INTEGRATION and REGULATION of METABOLISM

Part 1
INTEGRATION OF METABOLISM

General principles

1) There are several types of metabolism: CH, L, AA, and NA metabolism. But this division is conventional. These types of metabolism do not function separately from each other. Vice versa, they are **interrelated and integrated**.

- The anabolic and catabolic processes are interrelated.

Energy obtained from catabolic processes (degradation of molecules) is used for synthesis of molecules (anabolic processes).

- Substrates of one type of metabolism can be converted to substrates of some other type of metabolism, depending on the requirements of the organism.

2) The change in the concentration of a substrate causes the change of the velocity of metabolic pathways and intensity of metabolism.

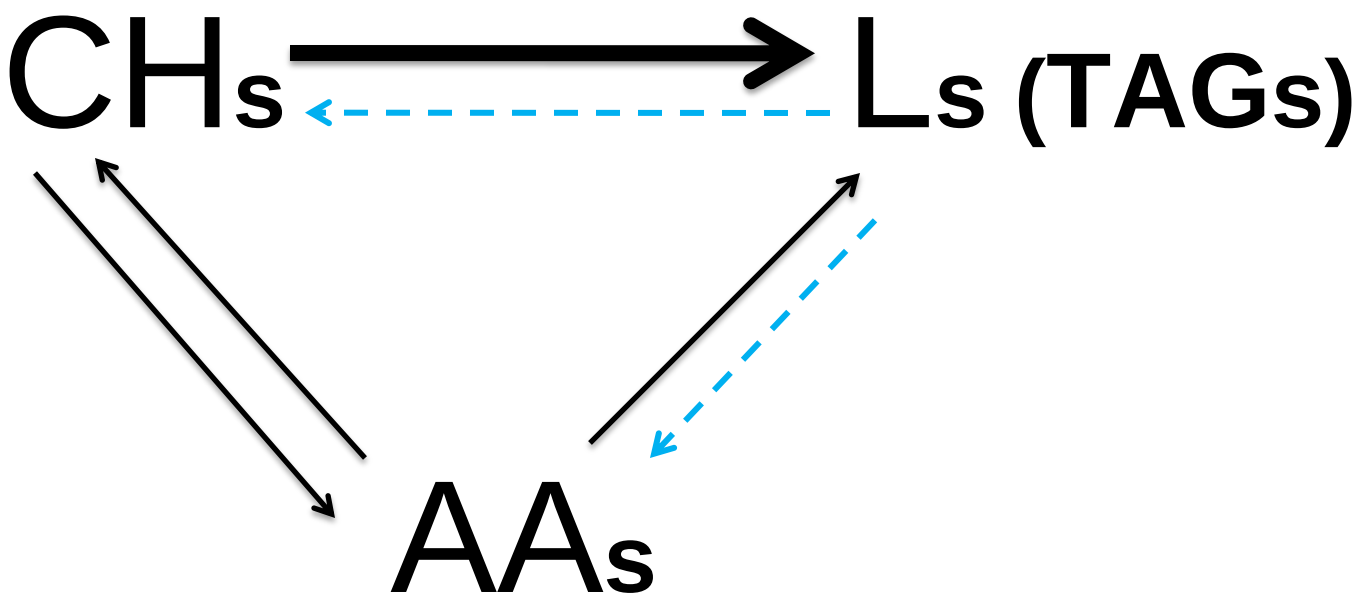
3) **Organism can maintain** adequate and **optimal level of metabolism** due to **regulatory** (control) **mechanisms**.

These mechanisms help regulate biochemical reactions and metabolic pathways, guide conversions of molecules to the appropriate direction and thus **maintain constancy of the internal environment (homeostasis)** of the organism.

Thus, integration and interrelation of metabolism implies:

- Anabolic and catabolic processes are interrelated;
- All metabolic processes in the organism are regulated by control mechanisms;
- Control mechanisms give appropriate direction to all metabolic reactions according to the body requirements.

Interrelation of metabolism

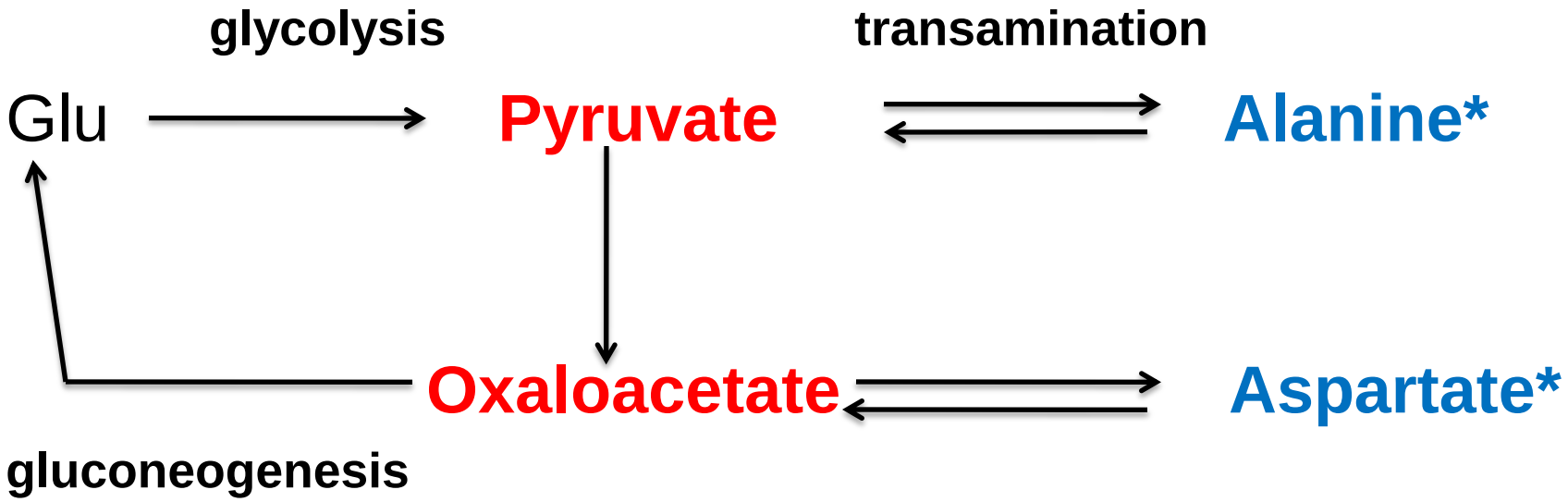


Interconversion of CHs and AAs

CHs ⟶ AAs (non-essential AAs)

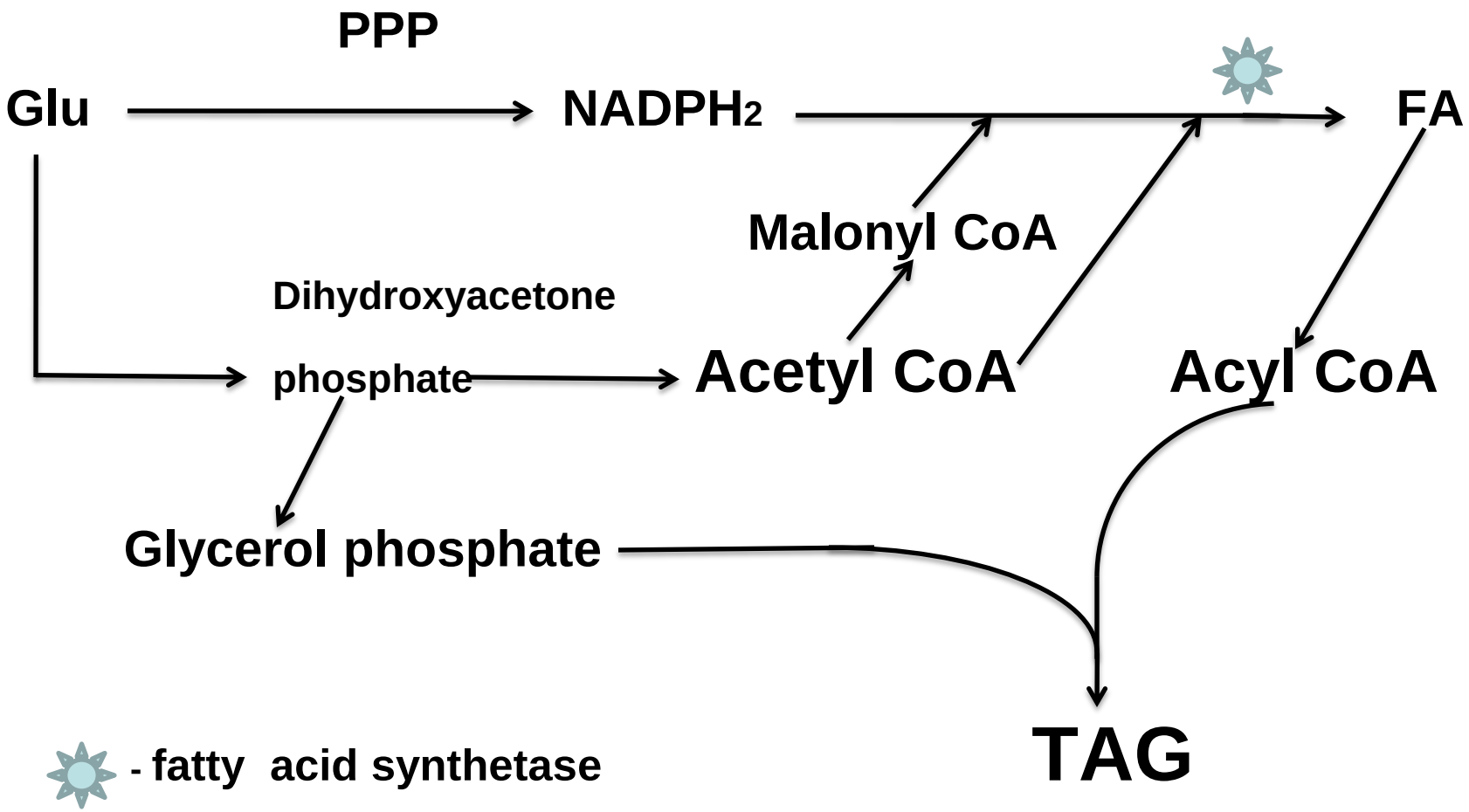
AAs (glucogenic AAs) ⟶ CHs

Scheme of interconversion of CHs and AAs



*** - glucogenic non-essential amino acids**

Scheme of conversion of CHs into lipids (TAG)



Conversion: L (TAG) ⟶ CH

TAG consist of **FA** and **glycerol**.

Neither FA, nor its active form acyl CoA,

nor acetyl CoA can be converted to glucose.

Only glycerol can be converted to glucose.

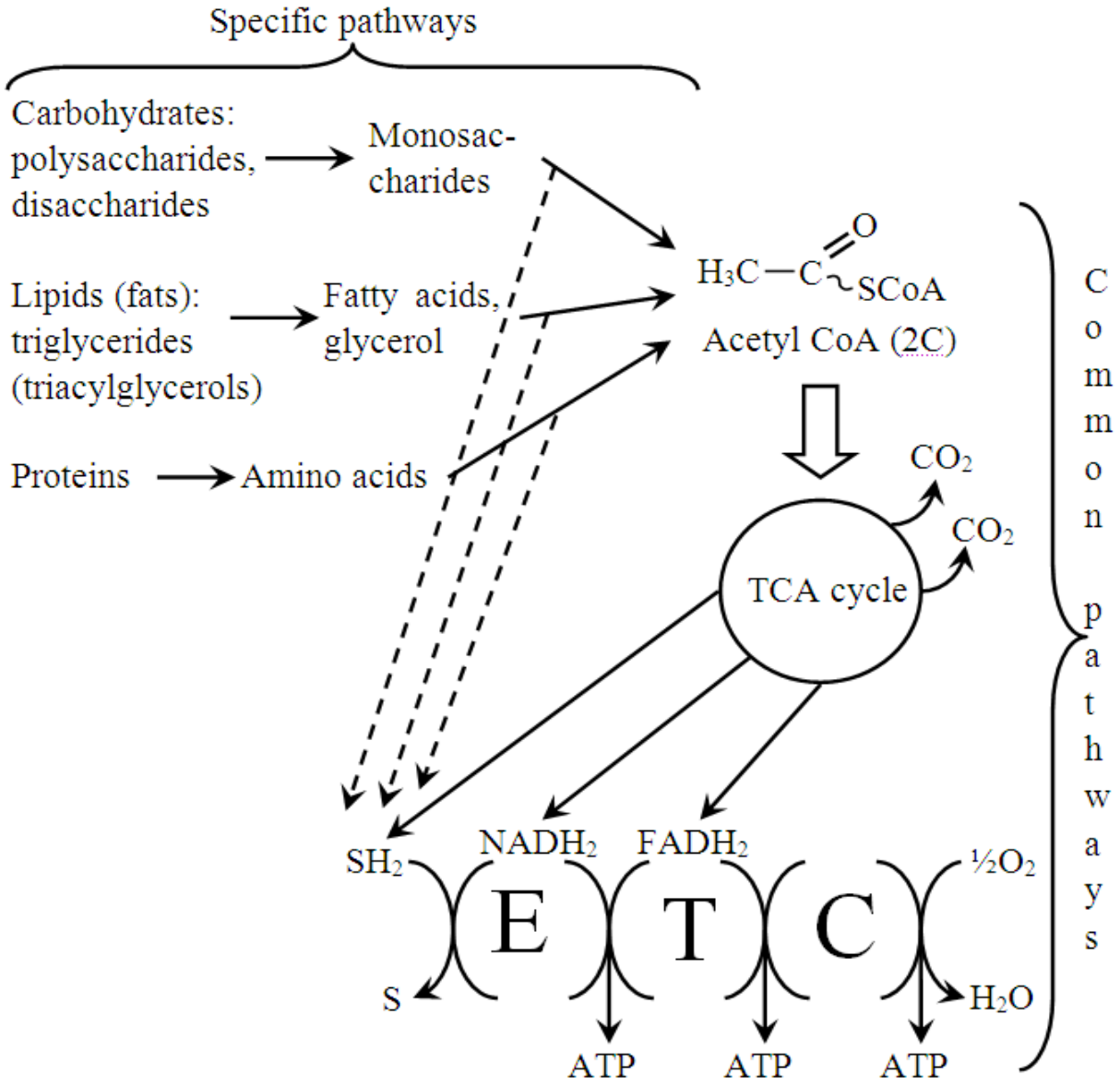
Conversion: AA ⟶ L

There are two groups of AA:

- **Glucogenic AAs** – they may be used for synthesis of **glucose**
- **Ketogenic AAs** – they form acetyl CoA (or acetoacetyl CoA) and may be used for **synthesis of KB, Ch, and FA**. Ketogenic AA: Lys, Leu, Phe, Tyr, Trp.

  Ser and Met may be used for synthesis of PhL.

SPECIFIC AND COMMON PATHWAYS OF CATABOLISM


Specific pathways
Carbohydrates: polysaccharides, disaccharides
Monosac-charides
Lipids (fats): triglycerides (triacylglycerols)
Fatty acids, glycerol
Proteins
Amino acids
H3C—C(=O)~SCoA
Acetyl CoA (2C)
CO2
CO2
TCA cycle
SH2
NADH2
FADH2
½O2
E
T
C
S
H2O
ATP
ATP
ATP
Common pathways

Specific pathways of catabolism.

Carbohydrates, lipids, and proteins of the human body or from the food are degraded to smaller molecules which are then converted to form acetyl CoA.

Common pathways of catabolism.

Acetyl CoA is utilized in the TCA cycle to form CO_2, reduced substrates (SH_2) and reduced coenzymes ($NADH_2$ and $FADH_2$). These reduced components undergo oxidation in the ETC to produce ATP.

Then ATP is used for synthesis of many compounds.

- **Integrating function of the TCA cycle**. All types of metabolism (carbohydrate, lipid and amino acid metabolism) can be interrelated through the TCA cycle by conversion of one types of substrate into others.

Part 2
Regulation of metabolism

There are two major principles of metabolism:

1) **Maximal thrift** (maximal economy). The organism avoids hyperstimulation or overproduction. The amount of substrates produced corresponds to requirements of the body at definite time.

2) Metabolic advisability (profitability).

In the organism, only those processes take place which are metabolically advisable (profitable).

(E.g., after meals, **synthesis** of glycogen takes place;

in starvation, **degradation** of glycogen takes place).

To support these two principles of metabolism, the control (or regulatory) mechanisms are used.

Role of regulatory mechanisms

- Regulate biochemical reactions;
- Guide conversions of molecules to appropriate direction;
- Provide optimal and adequate **rate** of metabolism;
- Maintain constancy of internal environment (homeostasis);
- Provide adaptation, adjust the organism to the changed living conditions.

Systems of regulation

1. **Nervous system** – with participation of CNS, PNS and neurotransmitters. This system does not cover all functions of all organs; therefore it is supplemented by
2. **Hormonal system** – participation of hormones.

   Nervous and hormonal systems provide coordination of all processes in the organism.
3. **Intracellular systems** – they involve **membranes**, **enzymes** and **genetic apparatus**.

Levels of regulation

Metabolism may be regulated on different levels:

- The whole organism;
- Separate organ;
- Cell;
- Molecular level.

Time of regulation

- 1. **Short-term** regulation (lasts for minutes or seconds) – the already existing molecules of enzymes are modified and, as a result, **activity of enzymes** is changed.
- 2. **Long-term** regulation (lasts for hours) – as a result, **quantity of enzymes** is changed.

Major regulatory **mechanisms**

The most important mechanisms of regulation may involve:

1. **Membranes**.

– the change of **membrane permeability** (insulin ↑ membrane permeability; glucocorticoids and GH↓ membrane permeability);

– **compartmentation**;

– membrane **receptors** (they bind with hormones).

2. The change of enzyme activity.

Metabolic pathways are controlled by key reactions catalyzed by regulatory enzymes.

Enzyme activity may be changed due to

– ↑ or ↓ of [S];

–cations and anions (cofactors, activators and inhibitors) ;

– coenzymes (derivatives vitamins);

– conversions of pro-Es into Es;

– phosphorylation-dephosphorylation of Es;

– allosteric effectors (activation by a precursor; retroinhibition).

3. The change of enzyme **quantity**

may be due to:

– **induction** (the increase of synthesis of protein or enzyme);

– **repression** (the decrease of synthesis of protein or enzyme);

– **increased degradation** of protein (enzymes).

The major inducers are nutrients or hormones.